# AN AMEBA-LIKE ORGANISM IN THE KIDNEYS OF A CHILD

WITH 2 PLATES

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The discovery of a protozoon invasion of the kidneys of a child who died suddenly in a convulsion while seemingly not in a serious condition seems worthy of description.

A colored boy, 15 months old, entered the Durand Hospital on the evening of Sept. 1, 1921. He had a history of fever with swelling of the gums about the lower bicuspid teeth and accompanied by a convulsion on August 25, which lasted 15 minutes. He had never had a convulsion previous to this time. He seemed better for the next day, but on September 1 was worse again, and a physician was called who said something was wrong with the tonsils. The temperature was normal on admittance, and he did not appear especially sick but was drowsy. A throat culture was taken which later was reported positive for diphtheria bacilli. The following day was uneventful, the patient receiving the usual treatment for diphtheria. At 11 o'clock that evening he was sleeping well, and the pulse was reported good, but 20 minutes later he wakened while the temperature was being taken, began to cry, had a convulsion and died within a few minutes. No urinalysis had been made as a specimen of urine had not been obtained.

Anatomic diagnosis (Dr. Mulsow): Bronchopneumonia; enlarged mesentric lymphnodes; congestion and fatty changes of the liver; parenchymatous nephritis; edema of the glottis; accessory spleen.

Cultures of the heart blood and pericardical fluid on blood-agar plates and Loeffler's blood serum were sterile; cultures from the lung on the same mediums grew hemolytic streptococci.

The chief changes found in microscopic sections of the tissues are a mild edema of the lungs, small regions of focal necrosis in the spleen and some of the lymph nodes, and a parenchymatous nephritis. Whether the lesions in the spleen and lymph glands bear any relation to those in the kidney I am unable to state. They seemed to have an entirely different character, resembling the necroses found in diphtheria, and no forms resembling those found in the kidneys are seen. The changes in the kidneys are limited almost entirely to the epithelium of the

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tubules, being most marked in the tubules of the cortex. Only occasionally organismal forms are found in the glomeruli, but there are no observable alterations in them. In some of the secreting tubules the epithelial cells are almost totally destroyed or displaced by the round eosin-stained bodies (hematoxylin and eosin preparations) which first arrested attention. As in the case of a parasitic invasion of the salivary glands,[1] the tissue reaction is mild. There is little infiltration with leukocytes; a moderate number of plasma cells are present in places; the cells of the tubules seem to be partially or completely absorbed rather than destroyed by the action of the organism, and for this reason a casual glance at the section does not reveal the real extent of the damage.

In a well differentiated hematoxylin and eosin preparation the cytoplasm of the organism stains a deeper pink and is more granular than that of the kidney cells, and they are easily distinguished even with a rather low power lens. Stained with polychrome methylene blue without eosin the parasite stains a light robin's egg blue which readily distinguishes it from the deeper purplish blue of the kidney cells. With the Giemsa stain the organism takes a salmon pink color quite different from the bluish pink of the kidney cells and the distinctly yellowish red blood cells.

The forms assumed by the parasite are varied. Certain forms which have been interpreted as representing the schizogonic or vegetative form of the parasite are present chiefly in the outer portion of the cortex. The cells of some of the convuluted tubules are entirely displaced by small, round rather homogeneous bodies, 2-6 mikrons in diameter, nothing remaining except the cell walls (Fig. 30). Different stages in the development of the bodies are present in a tubule or even in a single cell. There are the small round bodies just mentioned, which are of fairly uniform size in the same group but differ considerably in size in the various groups or cells and are apparently simply confined by the epithelial cell membrane, while in other cells there are one or more bodies varying in size 10-18 mikrons in diameter, which contain small round bodies similar to those found free in the cells but in various stages of development. Frequently the large bodies appear to be without nuclei but nuclear fragments are frequent or a dimly outlined nucleus seeming to indicate that a nucleus is probably always present but is to a greater or less extent used up in the development of the small bodies. When the development of the large body or

[1] München. med. Wchnschr., 1904, 43, p. 1905.

schizont is complete, the limiting membrane disappears, and the small bodies become free in the kidney cell where they continue their growth. There is a considerable variation in the depth of stain taken by these bodies, some of them staining decidedly purplish while the majority are pink. With some stains they appear quite homogeneous but with others they are granular, especially about the periphery; even with the same stain there may be some difference in this respect. As before intimated, these smaller forms are regarded as merozoites since it seems that through their development a continuous reinfection of the host is brought about.

Another form which is quite numerous and more widely distributed than the former is a nucleated body which may be round, oval or quite irregular in shape, with a coarsely granular cytoplasm and a relatively small, deeply stained nucleus either eccentrically or centrally placed. These forms vary from 2 to 15 or 18 mikrons in diameter. The small nucleated forms are not very numerous (Figs. 1 and 2). Some have proportionately large nuclei with little cytoplasm while others have small deeply stained nuclei and much cytoplasm with few granules. These are usually found imbedded in the epithelial cells of the tubules but may be free in the lumen or in the tissues outside the tubules. From these forms there are all gradatious in size to bodies 15-20 mikrons in diameter, those about 12-15 in diameter being most numerous. These larger forms are also present both in the epithelial cells and in the lumen of the tubule and quite as often in the latter as in the former. They are sometimes found partly inside and partly outside of the epithelium and sometimes the main part of the parasite is still outside the epithelium while a finger-like process is apparently forcing its way into the cell. Such appearances seem to warrant the assumption that the organism possessed a certain amount of ameboid motion. Besides the difference in size there is considerable variation in appearance. They are often quite irregular in shape often with quite definite processes or pseudopods and frequently contain one or several round, definitely outlined bodies which in appearance and staining reaction resemble the merozoites described, but they are not present in such large numbers. Occasionally there appears to be one or more vacuoles, and in some of the larger forms there is present in the cytoplasm a circular, more lightly pink stained, granular, nonnucleacted body surrounded by a wide unstained halo.

The nucleus apparently undergoes many changes. Sometimes a small round mass of chromatin is seen budding off from the nucleus,

and occasionally this small portion of nuclear material may be seen entirely outside the mother cell but still attached to the nucleus by a thin strand of nuclear material. Rarely one sees a nucleus with 3 or 4 processes budding off and in various stages of separation (Fig. 8). There is generally a massing of the chromatin at various points in a nucleus concerned in this process. Little cytoplasm seems to be carried away with the buds. The small nucleated bodies so produced may be one source of the small nucleated bodies I have mentioned. There is also the somewhat larger nucleus usually with chromatin massed at the periphery which is seen in various stages of simple division (Figs. 5, 6 and 7). In some cases the nucleus is simply elongated and becoming slightly constricted at the middle portion without change in the contour of the cell; in others the cytoplasm is also being constricted, and in the final stage the two nucleated portions are seen connected by a thin threadlike strand of chromatin surrounded by a narrow margin of cytoplasm, making it apparent that the bodies reproduce by simple division.

Besides the nuclei just mentioned, there are those with no other apparent change than a rather symmetrical massing of the chromatin about the margin of the nucleus. There are often 4 masses of about equal size; sometimes there is also a central mass connected by narrow chromatin bands with the peripheral masses giving the appearance of a Greek cross; or the nucleus may be oval with a larger mass at either end and two smaller ones between them on either side; or there may be 8 masses of nearly equal size with a more or less symmetrical arrangement. One not infrequently sees two nuclei of this type apparently within the same body or two bodies of similar appearance lying in contact within a cystlike cavity in a kidney cell.

Nuclei apparently in the various stages of mitosis are numerous. They stain deeply and are quite irregular in shape. Among these are nuclei showing a more or less perfect spindle formation. There is elongation of the nucleus with heavily staining polar caps, the intervening portion staining more lightly and seemingly arranged in strands connecting the deeper stained terminal portions. In a number of instances organisms have been seen in the same stage of division described and illustrated by Janicki as occurring in Paramoeba chaetogathi [2] (Fig. 10).

Microgametes have not been identified in these sections beyond a reasonable doubt. Forms have been seen which resemble somewhat

[2] Handbuch der path. Mikroorganismen, 1913, 7, p. 59.

microgametocytes, but in no case have forms been seen with a structure sufficiently definite to be convincing. It seems, therefore, that we are concerned here with reproduction by antogamy rather than by anisogamy.

Encysted forms are fairly numerous (figs. 17-24). An apparently early form consists of a large granular body which contains a lightly stained but clearly outlined eccentrically placed cystlike body. It is separated from the rest of the body by a thick wall inside of which is a clear unstained space, and occupying the central part is an irregularly shaped not very deeply stained mass. The cytoplasm of these cells usually contain none of the small round bodies. Other medium sized forms 8-10 mikrons in diameter contain a lightly stained, round or oval cystlike body within which are 2 to 8 or 12 small round deeply stained bodies usually surrounded by a halo, which vary somewhat in size. The apparently fully developed cyst is oval and contains about 12 of the small bodies and is sometimes seen, freed from the granular portion, in the lumen of the tubule. Occasionally one sees these small bodies apparently freed from the cyst and surrounded by granular material, probably the remnants of the mother cell. If they become free in the kidney, as it seems likely they do, they may easily be one source of the small nucleated bodies before mentioned which have been looked on as gametes.

In some of the large nucleated forms there is a fragmentation of the nucleus and a scattering of the nuclear material of the merozoits, although in some of the bodies which apparently give rise to merozoits no trace of a nucleus is found.

It is interesting to speculate as to the part played by the kidney infection in the fatal issue in this case. Both from the clinical and pathologic points of view the diphtheritic infection does not seem to have been of sufficient severity to cause the sudden death, whereas the parenchymatous nephritis was marked enough to be observable in the gross specimen, and histologically the changes in the epithelium of many of the secreting tubules are striking, seemingly making symptoms inevitable. However, in view of our scanty knowledge of infection of this kind, it would be unwise to draw any definite conclusion.

Three reports of the presence of somewhat similar protozoon-like bodies in the kidneys have been found in the literature. In 1904, Jesionek and Kiolemenoglou [1] report finding large protozoon-like cells in the kidneys, liver and lungs of an 8 months syphilitic fetus. These cells were 20-30 mikrons in diameter with large nuclei and granular

cytoplasm. In the kidneys they usually occurred in groups and sometimes in tubular formation with surrounding connecting tissue forming a kind of capsule. These cells showed no genetic relationship to the body cells and are therefore not to be regarded as modifications of them. R. Hertwig also examined the specimens and expressed the opinion that these bodies were protozoa probably to be classified among gregarines.

Later in the same year, encouraged by this report, Ribbert [3] reports 3 cases in which similar bodies were found. In 2 cases these were in the parotid glands of 2 young children neither of whom were syphilitic, and in the third case in the lumen of the tubules in the kidneys of a new-born syphilitic child. The tubules containing these cells were dilated and the epithelium considerably changed. The bodies were not seen outside the tubules in the connective tissue or in the glomeruli or collecting tubules. They had large homogeneous nuclei with nucleoli and between the nucleus and protoplasm was a clear zone as though the nuclear material had contracted and separated itself from the nuclear membrane. The author thinks that the location of the bodies in the lumen of the tubules speaks against their being body cells and that their presence in injured tubules suggests some connection with the injury. He cites Ehlers and Rhumbler as not venturing to decide what the bodies were, being of the opinion that their morphology spoke neither for nor against their being protozoa and suggesting that they might belong among ameba or sporozoa on account of the character of the nucleus and their location.

Smith and Weidman [4] found peculiar cells in the kidneys, liver and lungs of an apparently full term dead fetus in which there was no maceration and the tissues were in a good state of preservation. The mother's history was negative both prior to and after the birth of the fetus. In the kidneys there were minute foci of leukocytes in the interpyramidal cortex, chiefly of mononuclear cells with a few polymorphonuclears. Large prominently nucleated cells occurred in dilated tubules within these foci. These cells were coarsely granular, round or oblong, pyriform or irregular in shape and about 38x25 mikrons in their diameters and possessed short thick pseudopods. The nuclei were relatively large, ⅓-½ the diameter of the cell and without evidence of nuclear division. Some forms were apparently without nuclei and encysted forms were present. The authors believed the parasite was an ameba but did not classify it among known forms, and the name Entamoeba mortinatalium was suggested.

[3] Centralbl. f. allgem. Path., 1904, 15, p. 45.
[4] Univ. Penn. Med. Bull., 1910-11, 23, p. 285.

The bodies found in these cases, while agreeing in some respects with the ones described by me, are somewhat larger, vary less in size, and present much fewer variations in form. It seems probable, however, that in all of these cases we are dealing with organisms of similar nature. In a careful examination of the literature on protozoa in the kidneys, in an effort to classify the organism, I have been impressed with its resemblance to ameba. Many of the forms observed make it evident that they move about by means of pseudopods and exhibit a great variety of form. Multiplication of the organism is brought about by simple division, schizogony and sporulation. Certain appearances also suggest that the parasite reproduces by autogamy. All of which points to at least a close relationship with ameba. A point of interest in these cases would seem to be that we are dealing with a condition which may have been frequently overlooked. The character of the organism is such that at a casual glance one might easily mistake them for body cells, especially if there has not been careful differential staining, as the leukocytic reaction is not very marked, as some of the nuclei resemble those of plasma cells and as the process is more one of absorption and replacement of the epithelium than necrosis of it.

## SUMMARY

An ameba-like organism, the apparent cause of an acute parenchymatous nephritis, was found in the kidneys of a child, 15 months old, who died suddenly in a convulsion. Neither the gross nor histologic examination of the tissues revealed any other apparently sufficient cause of death.

Three reports are found in the literature of the occurrence of somewhat similar organisms in the kidneys, twice in syphilitic fetuses and once in a stillborn, nonsyphilitic child.

The character of the organism and the nature of the reaction in the tissues are such that the condition might easily be overlooked.

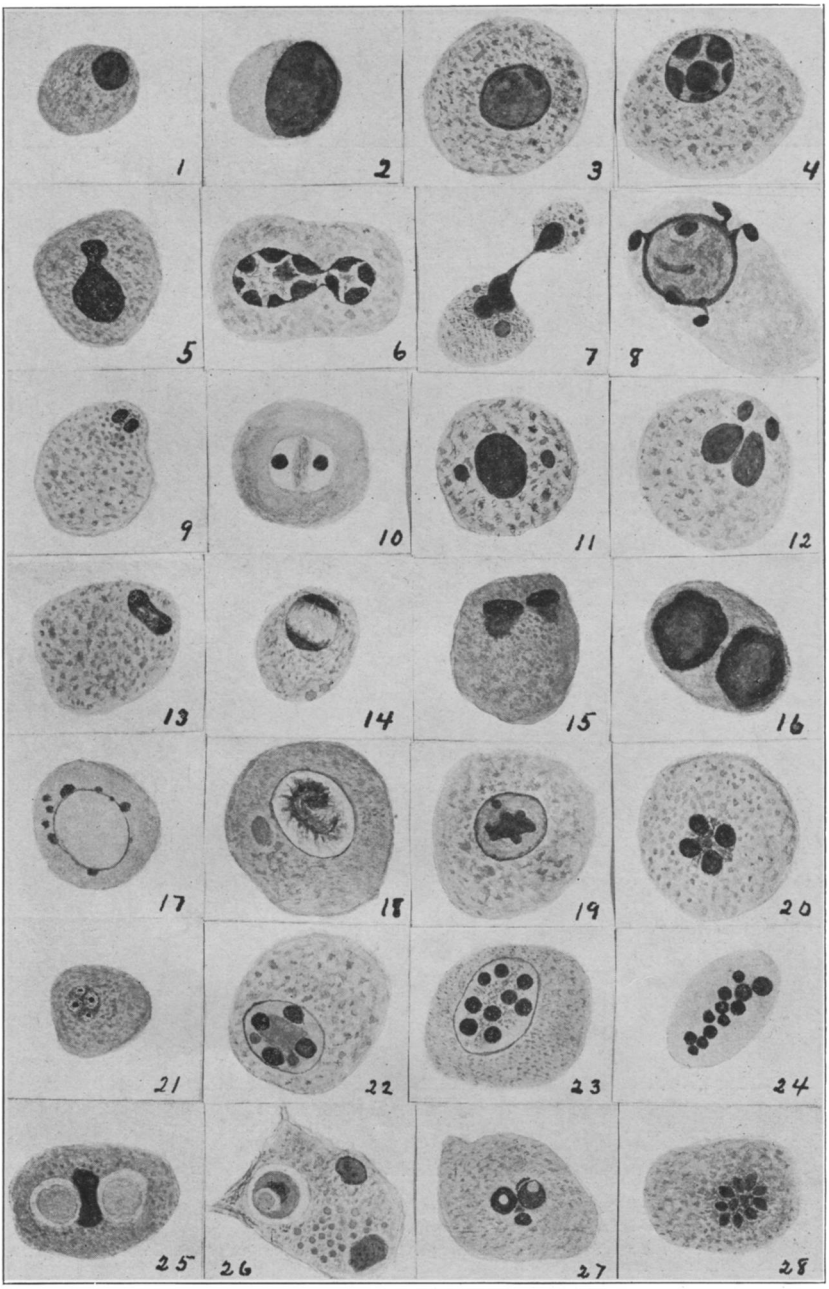


PLATE 1

Figs. 1-4.—Small and large stable forms of parasites.
Figs. 5-7.—Stages of simple binary fission.
Figs. 9-16.—Various forms of mitotic nuclei.
Figs. 17-24.—Encysted forms.
Figs. 25-28.—Unclassified forms.

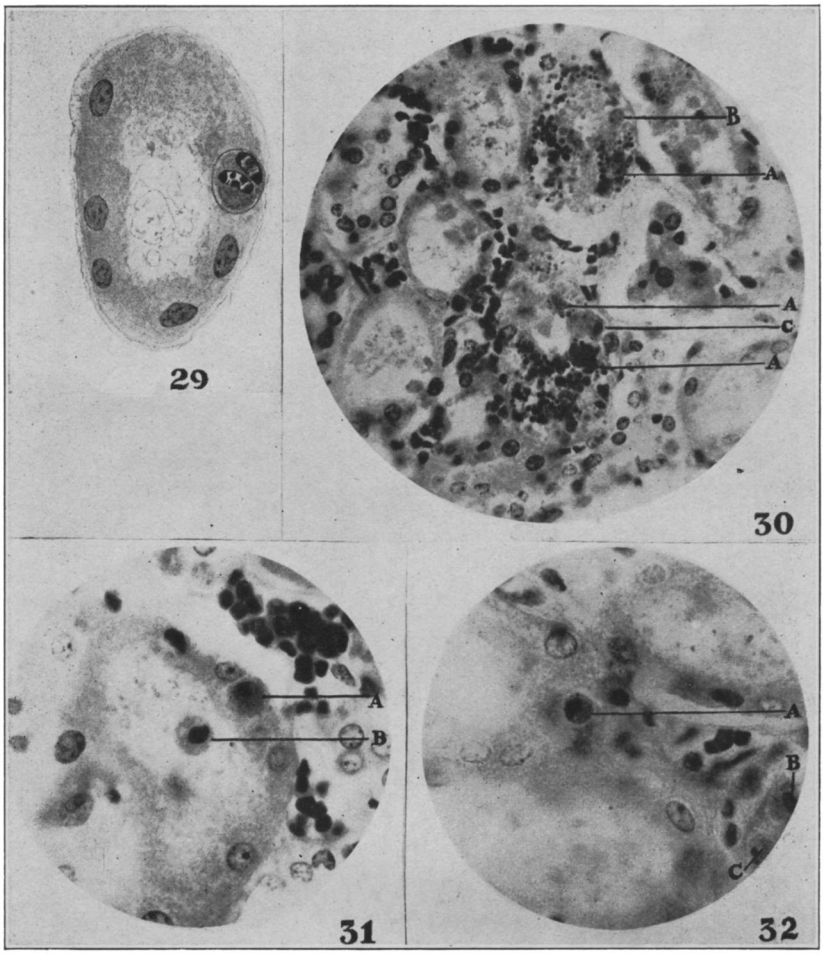


PLATE 2

Fig. 29.—Kidney tubule with a cystlike cavity containing two parasites of similar appearance.

Fig. 30.—Portion of the cortex showing tubular epithelium filled with schizogonic forms; *A*, merozoites; *B*, small nucleated form; *C*, large form; × 425.

Fig. 31.—Tubule containing two parasites; *A*, parasite within an epithelial cell; *B*, parasite in the lumen of tubule; × 780.

Fig. 22.—*A*, parasite in a tubular cell with nuclear material arranged in four round masses as illustrated in Fig. 20; × 780; *B*, parasite with large oval nucleus; *C*, parasite with small round nucleus.